



Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States

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The Management of Prenatal Care and General Principles of Antiretroviral Therapy and HIV Management in Women Who Were Infected Perinatally (Last updated October 26, 2016; last reviewed October 26, 2016)

Panel's Recommendations

- The management of prenatal care and general principles of antiretroviral therapy (ART) and HIV management do not differ between pregnant women who were infected perinatally and those who acquired HIV infection postnatally. With appropriate ART and prenatal management (and when optimal viral suppression is attained) the risk of perinatal transmission does not appear to be increased in women who acquired HIV perinatally (**AII**).
- Using the same guiding principles that are used for heavily ART-experienced adults, optimal ART regimens should be selected on the basis of resistance testing, prior ART history, and pill burden (**AII**).
- The presence of extensive drug resistance may warrant the use of ARV drugs for which there is limited experience in pregnancy. Consultation with experts in HIV and pregnancy is recommended (**AIII**).

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

With the availability of potent antiretroviral therapy (ART), morbidity and mortality have significantly declined in HIV-infected individuals, including those with perinatally acquired HIV. An increasing number of those who were perinatally infected with HIV are now reaching childbearing age and becoming pregnant. A significant number of these pregnancies are unintended.¹⁻³ The components of prenatal care and general principles of ART and HIV management do not differ between pregnant women who were perinatally infected and those who acquired HIV infection in other ways. However, there are unique challenges in this population related to reproductive health care needs and the prevention of perinatal transmission. Adherence to ART is commonly a major challenge for perinatally infected women. In addition, because most perinatally infected pregnant women are adolescents and young adults, they may be at higher risk of certain pregnancy complications such as preterm delivery, low birthweight, and preeclampsia.⁴⁻⁸

Antiretroviral resistance rates have been reported to be as high as 30% to 50% in perinatally infected pregnant women.^{8,9} This is due to extensive ART exposure prior to pregnancy, including exposure to suboptimal monotherapy or dual-therapy regimens as children.⁸ Optimal ART regimens should be selected on the basis of resistance testing, prior ART history, and the same guiding principles used for heavily ART-experienced adults. Consideration should be given to regimens that optimize dosing intervals and minimize pill burden. Consultation with experts in HIV and pregnancy is recommended.

Studies comparing perinatally and horizontally infected (e.g., through sexual contact or injection drug use) pregnant women have reported that perinatally infected women are more likely to have lower median CD4 T lymphocyte counts, detectable viral loads, and genotypic drug resistance (40% vs 12%).^{8,10} In a retrospective analysis of 37 pregnancies among perinatally infected women and 40 pregnancies among age-matched horizontally infected women delivering during the same time period, the viral load decline achieved during pregnancy in the perinatally infected women was not sustained during postpartum follow up in contrast to the horizontally infected women. During 4 years of follow up, there were 4 deaths due to AIDS-related complications in the perinatally infected women and none in the horizontally infected women.¹⁰ Although genotypic mutations were more common in perinatally infected women, loss of viral suppression resulting in progression of disease postpartum was more likely related to adherence, highlighting the need for special focus on adherence interventions after delivery.

Study results have been conflicting as to whether perinatally infected women have elevated rates of preterm and small-for-gestational-age (SGA) infants when compared with horizontally infected women. Williams et al reported a 31% incidence of preterm delivery and/or premature rupture of membranes in a cohort of

10 perinatally infected pregnant women.⁹ In a cohort of 79 pregnant women (17 with perinatal and 62 with horizontal infection) with 87 live births, Jao et al reported a four-fold increased risk for SGA births among the women infected perinatally.¹¹ Munjal et al reported perinatally infected women were more likely to deliver at an earlier gestational age and their infants had lower average birthweights than horizontally infected women.¹⁰ In contrast, Agwu found no differences in adverse pregnancy outcomes in 96 pregnancies between perinatally and horizontally infected women; however, there were high rates of preterm births in both groups (29.4% among women with perinatal infection and 36.3% among those with horizontal infection).¹² Badell et al did not find differences in birth outcomes between 20 women with perinatal infection and 80 with horizontal infection.⁸ Jao et al compared the growth patterns in the first year of life between 152 children born to perinatally HIV-infected as compared to horizontally infected women in the United States. The infants born to the perinatally infected women had lower mean length for age throughout the first year of life.⁷ Several studies have suggested that perinatally infected pregnant women are more likely to have a cesarean delivery most commonly related to prevention of HIV infection due to lack of optimal viral load suppression.^{9,10} Cesarean section in these young women raises concerns for increased risk of adverse obstetric outcomes if repeated cesarean sections are required for future pregnancies. Reassuringly, despite prolonged HIV infection, receipt of multiple ART regimens, and increased likelihood of having drug-resistant virus in perinatally infected women, with appropriate ART, prenatal management and when optimal viral suppression is attained, the risk of perinatal transmission does not appear to be increased in this population.^{8-10,13-15}

Among perinatally infected adolescents, pregnancy may create additional burdens in the transition from pediatric/adolescent HIV care to adult care. Psychosocial challenges may be magnified due to the presence of a lifelong chronic illness, high rates of depression,¹⁶ and frequently the loss of one or both parents. Attention to developmentally appropriate adherence counseling is critical. A systematic review and meta-analysis of 50 eligible studies on ART adherence in HIV-infected individuals aged 12 years to 24 years, in which adequate adherence was defined as greater than 85% by self-report or undetectable viral load, reported 62.3% adherence overall among HIV-infected youth. Youth from U.S. studies had the lowest average rate of adherence, at 53%.¹⁷ Sheth et al found that a history of depression was associated with nonadherence to ART among pregnant women who were perinatally infected.¹⁸ Focused attention on diagnosis and treatment of depression in the preconception period may lead to more optimal medication adherence. Kim et al found that self-motivation and social support were key to medication adherence in an HIV-infected adolescent population in the UK.¹⁹

Coordination of care across multiple disciplines including HIV primary care, ob/gyn, and perinatal case management is advised. Integration of reproductive health counseling and pregnancy prevention including consistent condom use and developmentally appropriate skill building to support disclosure are all recommended.

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